BUILDING A DATABASE FOR NANOMATERIAL EXPOSURE

by

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EXECUTIVE SUMMARY

Nanomaterials is a type of material with more advanced properties than conventional materials, and both scientists and engineers have a strong motivation to apply them in lots of areas. However, before they are widely applied, it is necessary to understand their toxicity on organisms. To date, large amounts of studies have explored the toxicity of nanomaterials, and they have greatly helped people understand how nanomaterials impact organisms. However, the developing speed of this field is getting slower because it is becoming more difficult for researchers to effectively search for information they need.

Building a user-friendly database for nanomaterials and bioactivity is the main objective of this project and it is also an effective solution to address this problem by strengthening the information dissemination in this field. Based on the basic database structure developed by researchers in the Center of Environmental Implications of Nanotechnology (CEINT), exposure data for carbon nanotubes (CNTs) will be collected and imported into the database, and in the meanwhile, the database structure will be further optimized to fit new dataset imported.

The method of this project is based on five steps:

1. Finding related studies and sources.
2. Extracting data from sources.
3. Preparing source files for the database.
4. Imputing data into MySQL database.
5. Query data from the database.

The database consists of six sections:

1. Materials section: Recording the properties of nanomaterials tested in each study.
2. Environmental System section: Describing the environmental system in which the study was conducted.
3. Biological System section: Recording information about the organisms chosen to conduct exposure experiments.
4. Functional Assay section: Recording the assay that provides a parameter that can be used to describe fate or effects of nanomaterials exposure.
5. Study section: Serving as the main section to connect each previous part and functionalize the whole database.
6. Study_PI_Publication section: Recording information about primary investigator and publication, and connecting this information with Study table.

Based on this database structure, I have imported data from 21 studies for CNTs into the database. The whole database works well and several applications have been developed. In my project report, two applications are introduced in detail.

Application #1: The impacts of exposing the same organism to different CNTs.

Different CNTs usually have different impacts on the same organism. However, most of studies usually focus on one of more types of CNTs. It would be a time-consuming process to review all published papers to understand how organism responds to different CNTs exposure.

Building a database is an effective way to help reduce time for searching data. In this project, I targeted at C.elegans as an example to show this application. As a result, C.elegans were exposed to three types of CNTs, and about 359 functional assays were found. Further analysis was conducted based on this selected data.

Application #2: The impacts of exposing the same type of CNTs to different organisms.

The Same type of CNTs may have different impacts on different organisms. The database is a useful tool to help address this issue. In this project, I wanted to know how single wall carbon

nanotubes (SWCNTs) influence different organisms. As a result, among all the dataset stored in my database, there were six organisms were exposed to SWCNTs and considerable amount of functional assays were conducted post SWCNTs exposure.

However, currently, the impacts of exposing the same CNTs to different organisms are incomparable, because of following reasons. The first one is that CNTs used in each study is not completely the same, although they are called with the same name. The second is that, due to the limited amount of data, all functional assays are different, and it means that simple comparison is not available to know which organism are more vulnerable to CNTs exposure.

This report also provides several key points of the database and recommendations to make a better database for nanomaterials exposure and boost the development of the field of nanomaterials safety.

1. The database can help researchers to avoid doing redundant studies and strengthen the communication between them. Moreover, it is a different search engine by focusing on specific study instead of keywords that is applied by conventional search method

2. The database structure should be further optimized in order to better fit the newly imported dataset.

3. The data quantity can be further expanded by developing a platform for database users to self-report their data.

4. Designing a series of standards for conducting exposure experiment and nanomaterials manufacturing will help to make the results of different studies more comparable. It is also an effective way to help increase the usability of dataset imported into the database.

5. Designing a series of indices, which include results of some normal tests (e.g. biouptake, death rate) and other important biomarkers. Based on analyzing these indices, a model can be built to evaluate the toxicity of exposing a certain type of nanomaterial to an organism.

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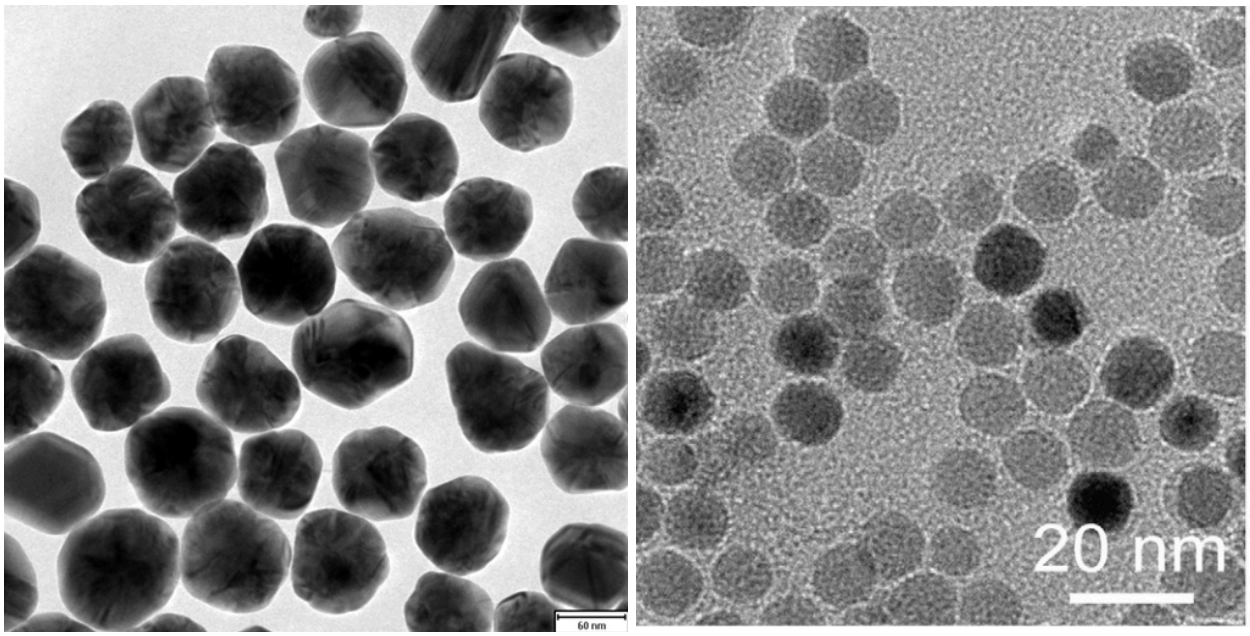
1 Introduction

1.1 Nanomaterial

Nanomaterial is widely defined as the substance with one or more dimension between approximately 1 and 100 nanometers (Arndt, D., 2014). The most commonly studied nanomaterials include silver nanoparticles, iron oxide nanoparticles, titanium dioxide nanoparticles, carbon nanotubes and graphene (EPA, 2014). By using nanomaterial, nanotechnology has been proved to be effective in several fields, such as environmental engineering (Debecker, 2014), chemistry (Weetall, H. H., 1999) and material science (Aitken et al., 2006). Figure 1 shows a transmission electronic microscope (TEM) picture of silver nanoparticles and iron oxide nanoparticles, where we can see the structure of two nanomaterials.



Silver Nanoparticles Iron oxide nanoparticles

Figure 1. TEM picture of silver nanoparticles and iron oxide nanoparticles. Source: Blue nano., (2014); Thaler et al., (2011)

The size of material is important to influence some of their properties, which are very different compared with normal and nano size material with same core substance. For instance, the nanoparticles have better ability in adsorption, absorption and radiation (NNI, 2014), for which the main reason is that nanomaterials usually have larger surface area, which also means they are more reactive. A single comparison shown by National Nanotechnology Initiative (NNI) is that for the same volume of particle (10^{-6} m^3), the surface area of nanoparticle (cube with side

length of 1nm) is 10^7 larger than the normal particle (cube with side length of 1cm). The larger surface area provides the nanoparticle a larger reactive area.

1.2 Carbon nanotubes

Carbon nanotubes, which were first discovered by Iijima (1991), are an important type of nanomaterials. The Single-wall carbon nanotubes (SWCNTs) and multi-wall carbon nanotubes (MWCNTs) are two main types of CNTs (Lu et al., 2010), and both of them share the hollow graphite cylinders structure (Iijima, 1991). Their structures are shown in the Figure 2

CNTs have been found equipping with several advanced properties compared with normal size carbonaceous materials, such as better mechanical strength, electrical conductivity, and bigger surface area (Baughman et al., 2002). Due to their outstanding properties, CNTs have been successfully applied in an increasing number of fields, such as energy storage (Che et al., 1998), drug delivery (Bianco et al., 2005) and chemical sensor (Penza et al., 2004).

For this project, data has been mainly collected for CNTs exposure.

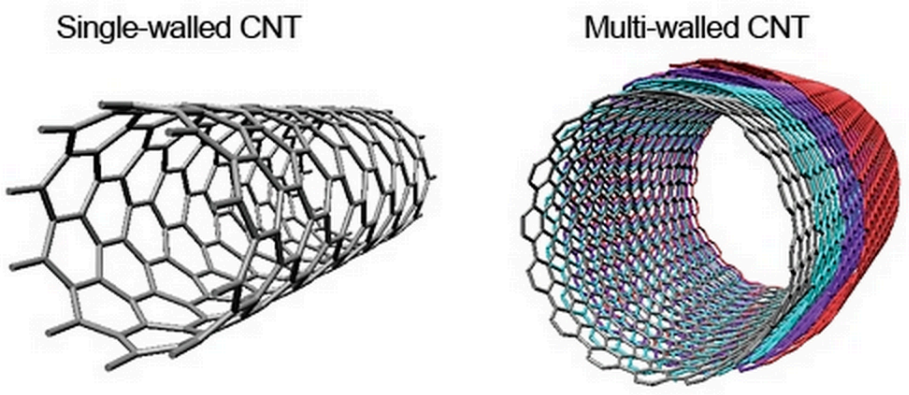


Figure 2. Structure of SWCNTs and MWCNTs. Source: University of Waterloo, (2015)

1.3 Risks induced by nanomaterials (e.g. CNTs) exposure

Although industry has a strong motivation to apply nanomaterials, before spreading them into every corner of our life, it is necessary to fully understand their toxicity on organisms, such as animals, human beings, plants and microorganisms. A considerable amount of toxicological tests have been conducted in order to explore how nanomaterials impact living organisms. For example, based on current studies, CNTs are found to have slight negative impacts on vertebrates and invertebrates (e.g. C. elegans, mammals and fish); however, positive responds have been detected on some species of plants (e.g. alfalfa and wheat) (Miralles et al., 2012; Wu et al., 2013;

Cheng et al., 2007; Pietroiusti et al., 2012). For the purpose of reducing the impacts induced by CNTs exposure, several solutions have been developed, such as surface functionalization and adding structural defects (Liu et al., 2010; Zhao et al., 2011).

On the other hand, discrepancies exist in the research methods and findings regarding the toxicity of nanomaterials. For example, regarding impacts on wheat, Miralles et al. (2012) and Wang et al. (2012) reached different results on whether MWCNTs would influence the wheat germination percentage and have the ability to penetrate into the wheat. Several reasons are offered to explain these contradictory results. The first is due to the different CNTs being tested, and the second relates to the different treatment and experimental methods that are commonly applied in these studies. Therefore, it is necessary to develop standardized methods to analyze the toxicity of CNTs for the better comparison of different studies and understanding of the impact caused by CNTs' exposure.

1.4 Database for nanomaterial exposure

In addition to designing standardized experimental methods to analyze the toxicity induced by nanomaterial exposure, building a database for them, which as suggested by Center of Environmental Implication of the Nanotechnology, is another effective way to benefit the whole field.

Database is a collection of information, and it is well organized for users to rapidly search for the data they need (Fairfield, 2004). Therefore, there are several elementary advantages to develop a database for nanomaterial exposure. The first one is that users can acquire currently available information about the impacts of exposure to certain types of nanomaterials. In addition, it is useful to keep researchers from doing repetitive studies. Increasing number of applications and advantages can be developed and found after the better design of database structure and importing of larger amounts of data.

1.5 Objective

The main objective of this project is to build a user-friendly database for nanomaterials exposure and bioactivity, to make the information in the database easily queried by users and to encourage users to contribute the development of this database by adding new data inside. The researchers in CEINT have already designed the basic database structure, which will be shown in the results section of this report. One of my roles is to collect and input data on representative

nanomaterials, which are mainly for CNTs, into the database, and the other is to optimize the database structure, which can fit the new dataset curated from various studies.

2 Method

2.1 Finding related studies and sources

The resources are primarily collected from published, peer-reviewed literatures, industrial reports and unpublished scientific studies conducted by CEINT researchers.

2.2 Extracting data from sources

Based on the content of the database, there are two types of data, directly reported data and figures & tables that can be utilized. It is relatively convenient to input the directly reported data into the database; however, for the data loaded by figures and tables, an additional tool is needed. A tool called GraphClick is capable of extracting this type of data. Because the certain degree of error is involved in the process of data curating, these data show only the approximate value. Another way to acquire data with high precision is by directly contacting the original authors.

2.3 Preparing source files for the database.

Building an Excel file including every table and field, and properly inputting data into it.

2.4 Importing data into MySQL database

Inputting the data loaded by the Excel file into the MySQL database.

2.5 Query data from the database

Using programing language to query the data in the database.

3 Results

3.1 Database Structure

The whole database consists of six parts: Material, Environmental System, Biological system, Study_Pi_Publication, Functionalization assay and Study (Core). The reason for choosing these six parts is that they include the most important information to descript studies of nanomaterials exposure. Figure 3 shows the overall structural diagram of this database.

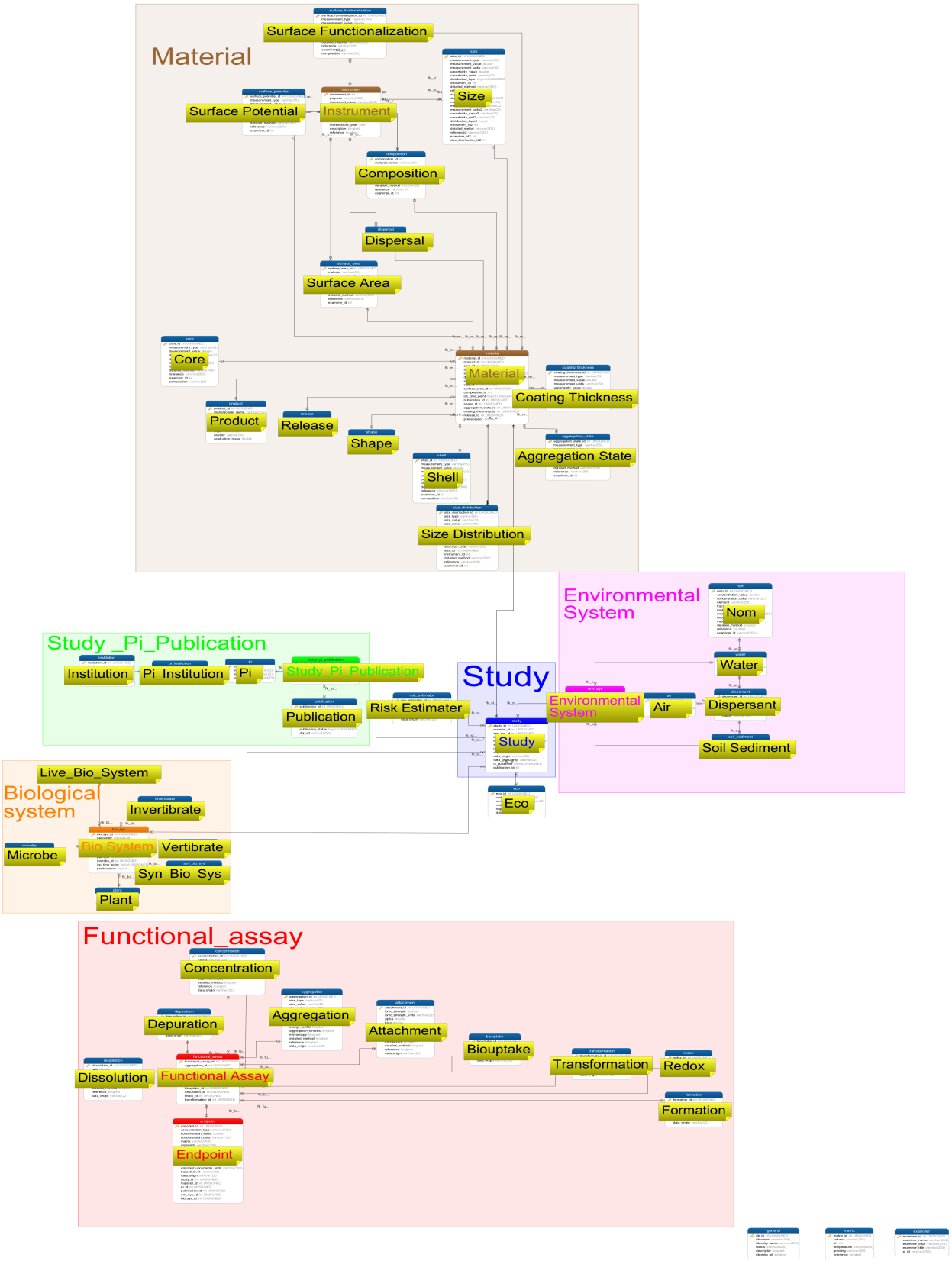


Figure 3. Database Structural Diagram

3.2 Main Structures

3.2.1 Material

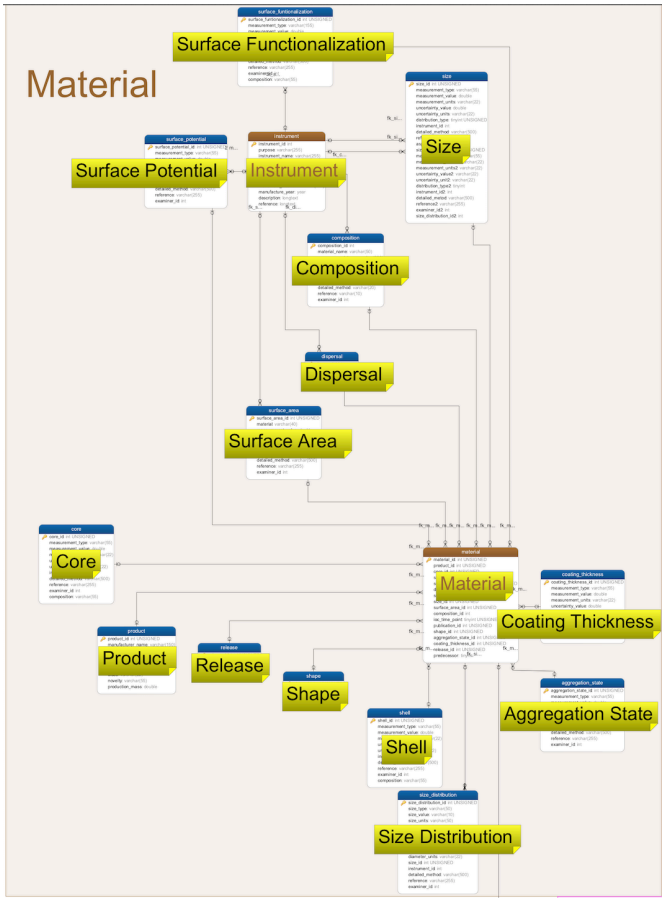


Figure 4. Structural diagram for material section

Material section stores data of the properties of nanomaterials tested in each study. The detailed structure for the Material section is shown in Figure 4. Figure 5 shows its simplified structure, in which tables are ordered in different levels. Higher order tables always acquire data from lower order tables. In this section, the second-order table is Material, which consists of thirteen third-order tables. Six of all the third-order tables connect with fourth-order tables. Moreover, the Size Distribution table is the only first-order table that acquires the data in the Material Table.

In the Material section, every third-order table represents one important property of nanomaterial. Table A in the Appendix shows the content of several tables, such as Size, Surface Functionalization, and Core.

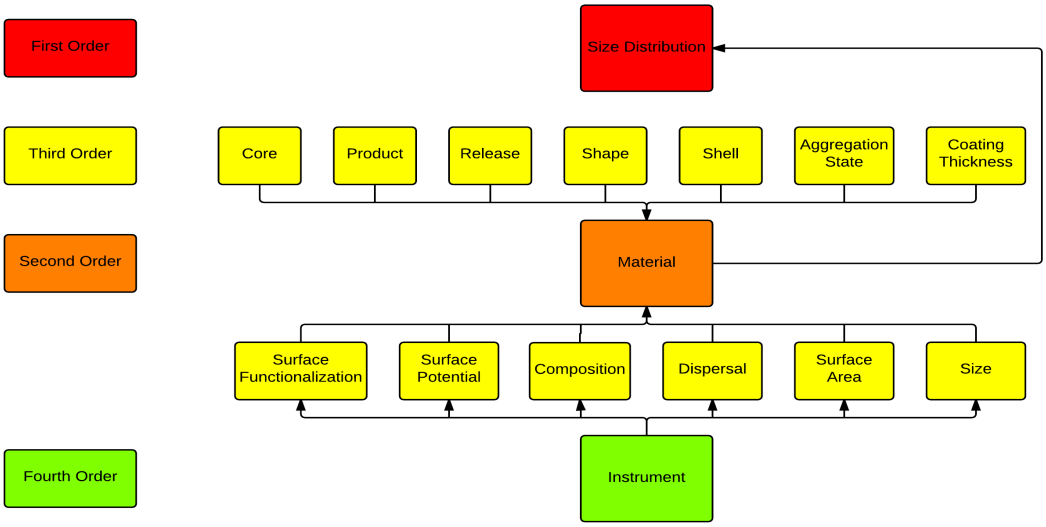


Figure 5. Simplified structural diagram for Material section

3.2.2 Environmental System

The Environmental System describes the environmental system in which the study was conducted. The Environmental System is the first-order table in this section, and the second-order tables include Water, Soil Sediment and Air. They are three types of experimental systems in which nanomaterials might be exposed to targeted organisms. The third-order table includes two parts. One is the Dispersant table, which is connected with three second-order tables, and the other is the Natural Organic Matter (NOM) table, which is connected with the Water Table.

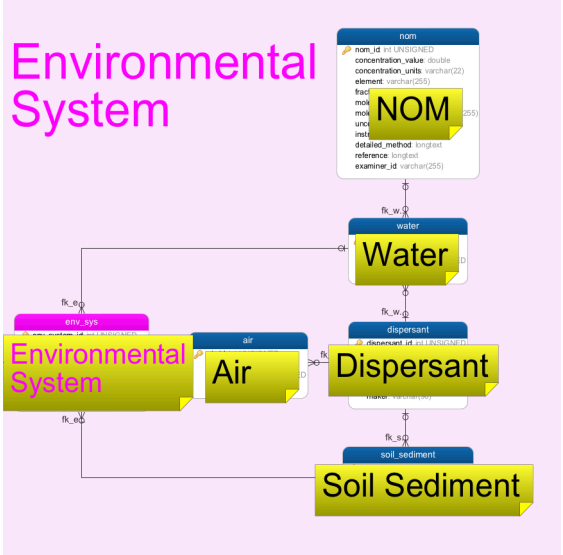


Figure 6. Structural Diagram for the section of Environmental System

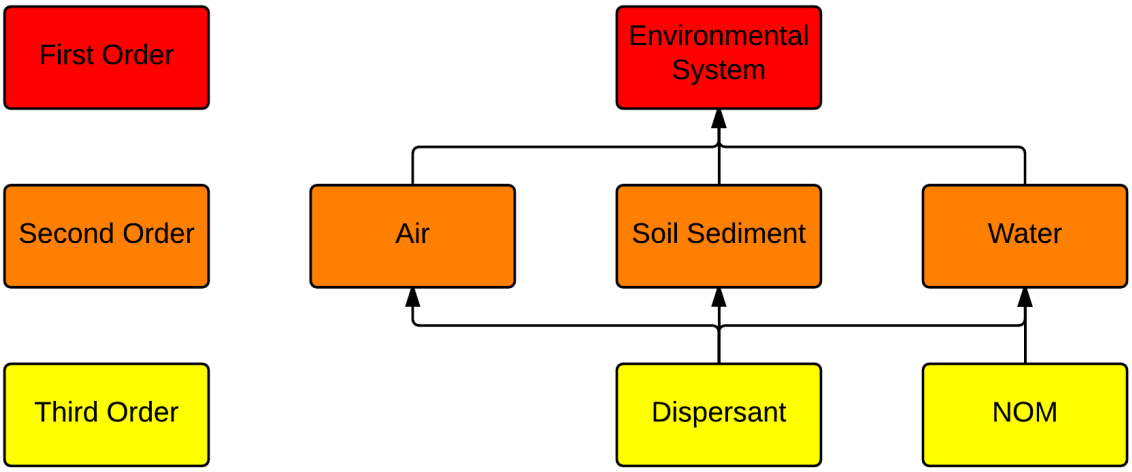


Figure 7. Simplified structural of Environmental System section

Figure 6 and Figure 7 show the structural diagram and simplified structure of this section, respectively. Table B in the Appendix shows the content of every table in this section.

3.2.3 Biological System

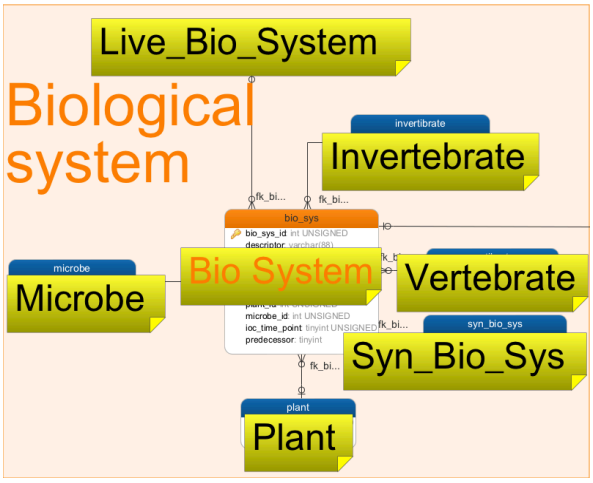


Figure 8. Structural diagram for the section of Biological System

The section of Biological System records information about organisms chosen to conduct exposure experiments. All six second-order tables in this section correspond six typical types of organisms that have been identified in the field of nanomaterial exposure. Figure 8 & 9 show the structural diagram and simplified structural of this section, respectively. Table C in the Appendix shows the content of four important tables in this part.

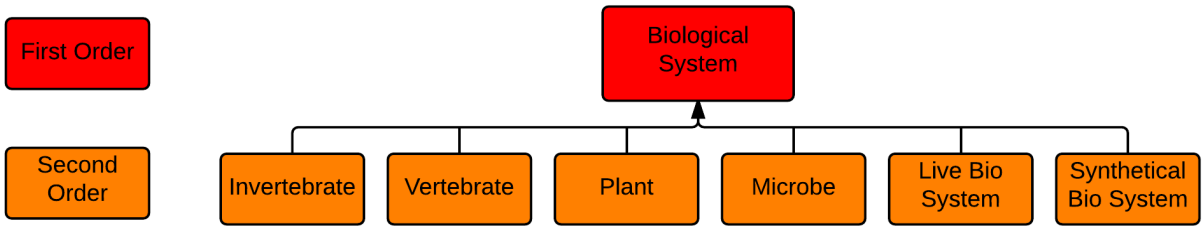


Figure 9. Simplified Structural of Biological System section.

3.2.4 Functional Assay

Functional Assay has been defined by Prof. Mark Wiesner and Prof. Greg Lowry in CEINT as "The assay that provides a parameter (not necessary fundamental) that can be used to describe fate or effects of nanomaterial exposure". In this section, Functional Assay is the only first-order table, and it is connected with ten second-order tables. In each study, the ending goal is different, and it is achieved by testing different parameters. In the database, it is inefficient to create second-order table for every parameter. Therefore, a table named Endpoint has been created to store these parameters. On the other hand, there are also several parameters regarded as the bulk indicators for some important biological processes and interaction between nanomaterials that Endpoint table does not cover. These other nine secondary tables are bulk indicators, whose parameters are not fixed. With more data going to be stored in the database, changes can be made on them. Figure 10 & 11 show the structural diagram and simplified structure of this

section, and the content of three selected tables (Functional Assay, Endpoint and Biouptake) are shown in Table D in the Appendix.

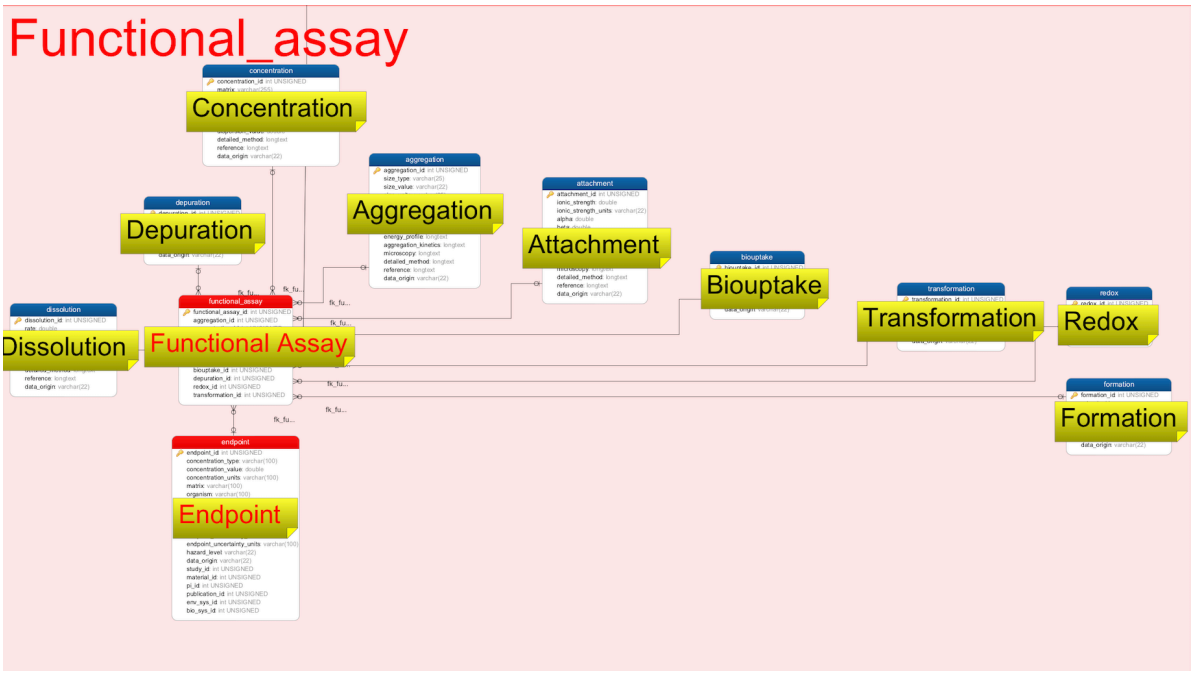


Figure 10. Structural Diagram of Functional Assay Section.

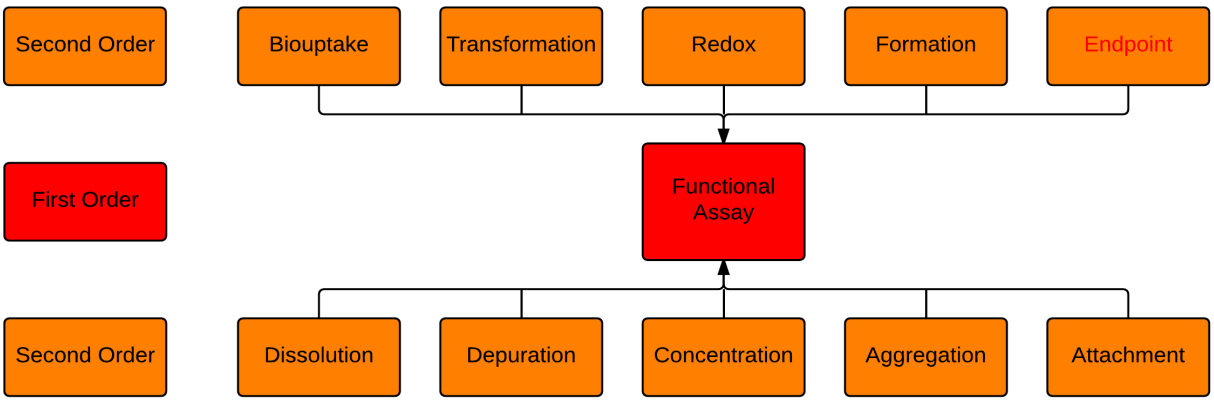


Figure 11. Simplified Structural of Functionalization Assay Section.

3.2.5 Study

All previous sections (Material, etc.) are independent from each other, and it is necessary to have a core table connecting with them to functionalize the whole database. A table named Study was created to serve this purpose and to connect all related information. The structural diagram and the simplified structural diagram for Study section are shown in Figures 12 & 13, respectively.

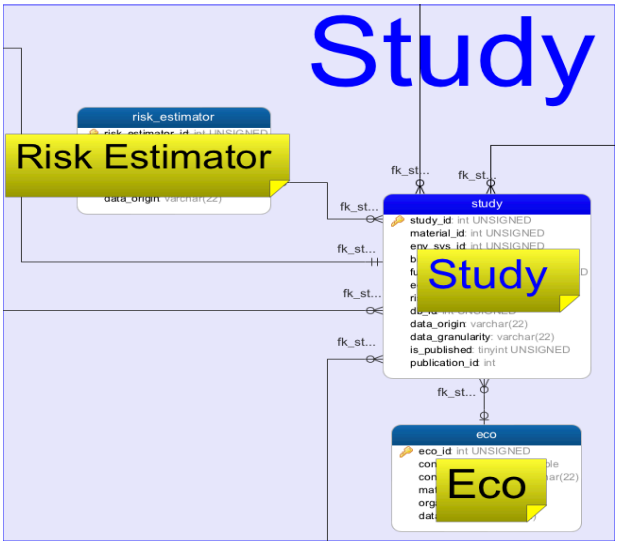


Figure 12. Structural Diagram of Study Section

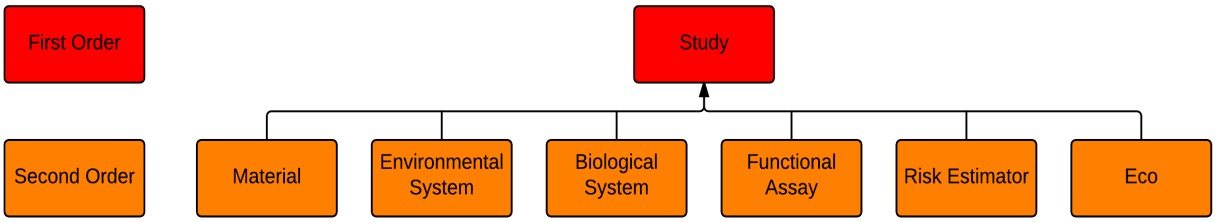


Figure 13. Simplified structural of Study section.

3.2.6 Sutdy_PI_Publication

Study_PI_Publication section records the authors' information: including the publication, primary investigator (PI) and their institution. In the database structure, it is the only section using data from the Study table, which means this section has the highest order in the whole database. Figure 14 shows the database's structural diagram of this section, and the simplified structural diagram is shown in Figure 15.

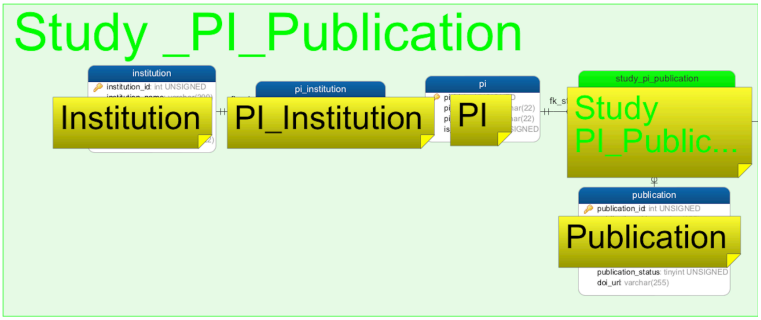


Figure 14. Database structural diagram for the section of Study_Pi_Publication

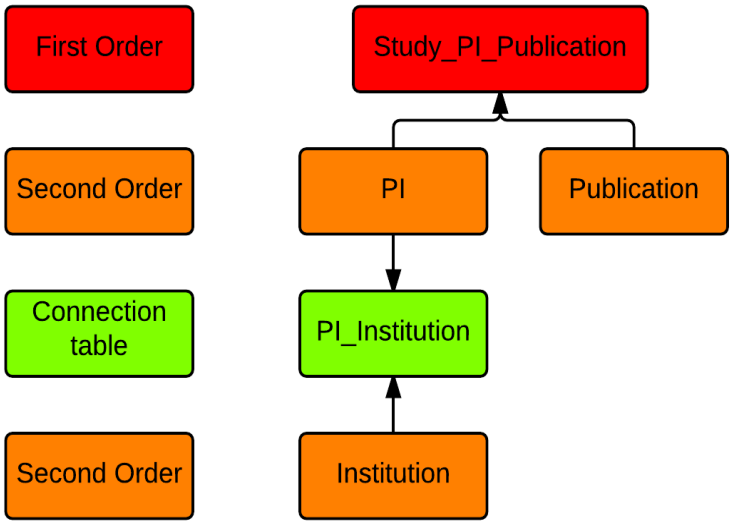


Figure 15. Simplified structure diagram for the section of Study_PI_Publication

Instead of making Institution a field in the PI table, it decreases the redundancy to make it a separate table with PI_Institution connecting both of them. For example, some PIs work for different institutions; thus, if the information of PI and Institution are stored in one table, redundant rows will be produced in both the PI and Study_PI_Publication tables. These redundant rows will make errors for data connection. Figures 14 & 15 show the structural diagram and the simplified structural diagram of this section, respectively. The content of all tables is shown in Table E in the Appendix.

3.3 Overview of Data Imported into the Database

The goal of this project is to curate data for CNTs exposure. Part II in the Reference shows the data sources, in which CNTs exposure data were extracted and imported into this database. Since it is unable to store a large amount of data into database at this initial stage of database building, attention should be paid to curate more data. In this project, 21 papers have been chosen based on the criteria of having diverse data covering more organisms and types of CNTs. The results show that three kinds of CNTs (MWCNTs, SWCNTs and FWCNTs) and four types of organisms, including vertebrates, invertebrates, plants and living biosystems (e.g., artificial skin, microorganisms) have been covered. Based on these data, some simple analyses can be conducted to get a deeper understanding of how CNTs affect organisms.

4 Application

Due to the data imported into the database, the application of it is currently focused on the CNTs exposure, and more applications can be developed after the database is further optimized.

4.1 Case #1: The impacts of exposing the same organism to different CNTs

How CNTs exposure impacts an organism is influenced by different factors, such as the type, size, surface functionalization and purity of CNTs, respectively (Cheng et al., 2007; Long et al., 2012; Chen et al., 2008; Miralles et al., 2012) and preparation methods for the experiment (Kwok et al., 2010). Most toxicological studies focus on one or more of these factors, which means it is a time-consuming process to review all published papers to understand how organisms respond to different CNTs exposure.

Building a database for nanomaterial exposure is an effective way to overcome this problem. For example, users can search for all data stored in the database relating to any targeted organisms. Table 1 shows the organisms with more than fifty functional assay items imported.

Organism Name	Number of items	Organism Name	Number of items
Seven-week-old male rats	712	Lolium multiflorum	77
Eight-week-old male Crl:CD(SD) rats	525	Barley hybrid Robust	72
C. elegans (Nematodes, wild-type N2)	359	Corn hybrid N79Z 300GT	72
Trout (Juvenile rainbow)	196	E. Coli K12 MG1655	72
Chlorella	139	Soybean hybrid (S42-T4)	72
Wheat (Triticum aestivum)	112	Zebrafish (Danio rerio)	68
T.japonicus	100	O.melastigma	65
Spinal cord of Leghorn chicken embryos	88	Daphnia magna	64
Dorsal root ganglia of Leghorn chicken embryos	84	Rat C6 glioma cell	60
Danio rerio	78	Mouse	51

Table 1. List of organisms with more than fifty functional assay items.

In Table 1, the number of functional assays conducted for “Seven-week-old male rats” and “Eight-week-old male rats” are the most among these organisms. On the other hand, the name for the same species of organism might be recorded differently. Therefore, it is necessary to search the exposure data for one species with several similar keywords.

4.1.1 Example: Targeting at C.elegans

“C.elegans (Nematodes, wild-type N2)” is chosen as the targeted organism to show this application, because it is the organism most frequently studied in the dataset currently imported into the database. Table 2 shows functional assays and CNTs that have been tested in each study.

Study #1		Study #2	
Type of CNTs	**Functional Assay**	**Type of CNTs**	**Functional Assay**
MWCNTs	Relative fluorescent intensity (intestine)	MWCNTs	Relative fluorescent intensity (intestine)
MWCNTs	Brood size	MWCNTs	Brood size
MWCNTs	Head thrashes/min	MWCNTs	Head thrashes/min
MWCNTs	Body bends/20 sec	MWCNTs	Body bends/20 sec
MWCNTs	Relative fluorescent intensity reflecting the production of reactive oxygen species	MWCNTs	Relative fluorescent intensity in intestine (comparison of ROS production)
MWCNTs-PEG	Relative fluorescent intensity (intestine)	MWCNTs-COOH	Relative fluorescent intensity (intestine)
MWCNTs-PEG	Brood size	MWCNTs-COOH	Brood size
MWCNTs-PEG	Head thrashes/min	MWCNTs-COOH	Head thrashes/min
MWCNTs-PEG	Body bends/20 sec	MWCNTs-COOH	Body bends/20 sec
MWCNTs-PEG	Relative fluorescent intensity reflecting the production of reactive oxygen species	MWCNTs-COOH	Relative fluorescent intensity in intestine (comparison of ROS production)

Table 2. Functional assay and to which CNTs that organisms have been exposed. MWCNTs-PEG: polyethylene glycol functionalized MWCNTs; MWCNTs-COOH: carboxyl functionalized MWCNTs. Source: Wu et al., (2013); Nouara et al., (2013)

Three types of CNTs, including raw MWCNTs, MWCNTs-PEG and MWCNTs-COOH, were exposed to C.elegans, and some functional assays were conducted in both studies, such as relative fluorescent intensity in the intestine, brood size, head thrashes and body bends. Users can decide how to analyze the data based on what kind of data is queried from the database.

Figure 16 shows some typical analysis based on existing data. In each functional assay, C.elegans were exposed to four types of CNTs with concentrations ranging from 0-1000 μg/L. The fluorescent intensity in the intestine is a valuable marker for the damage of aging cells (Wu et al., 2013). The results indicate that MWCNTs-PEG does not have obvious impact on the aging cells in the intestine; however, raw MWCNTs begin to have negative impact on C.elegans at concentration of 0.1 μg/L. Moreover, MWCNTs-COOH with a concentration higher than 10 μg/L will induce cellular damage, which also means it has lower toxicity than raw MWCNTs. Similar results have been found in the other three functional assays, which are synthetic indicators for the toxicity of CNTs. A conclusion that can be made on this synthetic analysis is that MWCNTs-PEG has the lowest toxicity toward C.elegans when the concentration of CNTs is higher than 10 μg/L. Among these CNTs, raw MWCNTs are shown to be toxic to C.elegans at the lowest concentration (0.01 μg/L) and to have the largest impacts on the target at the highest exposure concentration.

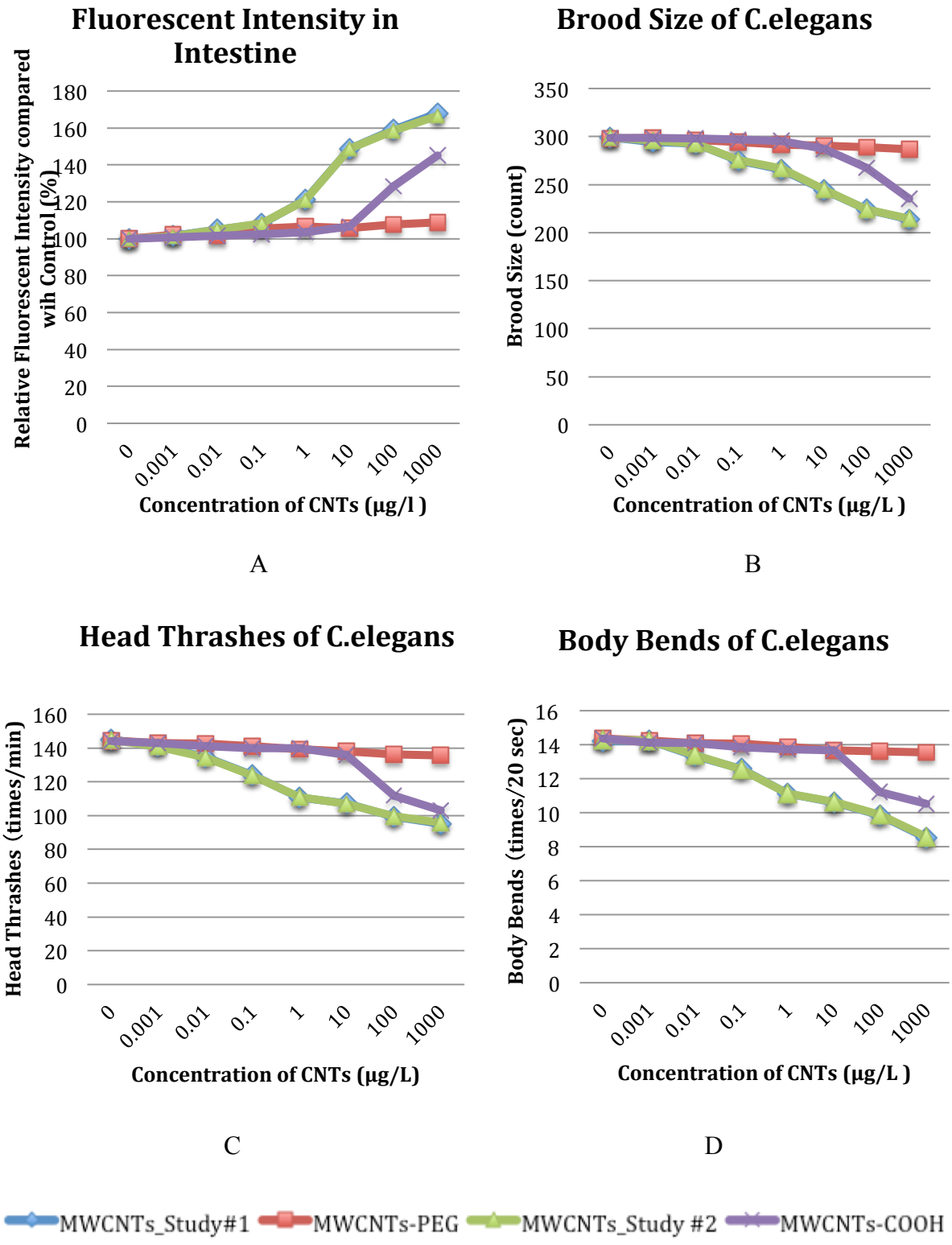


Figure 16. A. Fluorescent Intensity in Intestine; B. Brood Size of C.elegans; C. Head Thrashes of C.elegans; D. Body Bends of C.elegans. Source: Wu et al., (2013); Nouara et al., (2013).

4.2 Case #2: The impacts of exposing the same type of CNTs to different organisms

Different organisms respond to CNTs differently. For example, based on the data imported into the database, case #2 shows that CNTs do have negative impacts on most animals; however, these impacts generally are not serious enough to cause huge damages. On the other hand, positive effects have been found on plants after CNTs exposure. Therefore, it is hard to make a comprehensive conclusion toward the toxicity of CNTs. It is also difficult to compare the impacts induced by different CNTs exposure, because different functional assays were conducted for different kinds of organisms.

Building a database is an effective way to overcome this knowledge gap, because users can swiftly query the results of functional assays conducted for different organisms after specific types of CNTs exposure. How the same type of CNTs impact different organisms can be decided based on the analysis of these queried data. These results are very useful to understand which organisms are more vulnerable to the CNTs exposure. Furthermore, the results are helpful for fields like nanomaterials regulation and environmental restoration.

For example, Table 3 shows some functional assays for organisms that have been exposed to SWCNTs.

Organism	Functional Assay
Zebra fish (Danio rerio)	Hatching percent
	Head-Trunk Angle
Dorsal root ganglia of Leghorn chicken embryos	DNA content of mixed neuro-glial (% of control)
Epidermal JB6 P+ Cells	Viability
The skin of SKH-1 mice	Net Increase in Skin Bi fold Thickness
	Average cells per field
E. Coli K12 MG1655	Total Cell Growth (optical density)
	Biofilm Formation (optical density)
Mouse	Percentage of mouse with swollen uteri and no fetuses
	Percentage of mouse with at least one malformed fetus
	Contracting Embryotic Bodies (% of control)

Table 3. Organisms and functional assays that have been conducted on them.

Due to the current data stored in the database, the vulnerability of different organisms exposed to the same type of CNTs is incomparable. The main reason for this is that, in addition to various functional assays that have been conducted to show the toxicity of CNTs, the field of studying nanomaterial toxicity lacks a standardized functional assay that makes the toxicity of CNTs toward different organisms comparable.

On the other hand, although this comparison focuses on the same type of CNTs exposure, they actually are not the same CNTs, because different experimental conditions (e.g. functionalization and dispersal methods) are able to make CNTs with different characters. Therefore, it causes simple comparison between few studies to be less meaningful. Building a database with large amounts of data is a solution to minimize the influence of this problem, because it increases the possibility of finding enough toxicological data focusing on the same CNTs. However, it is not able to perfectly solve this problem, because extra effort needs to be spent on checking the original paper to make sure the same experimental conditions were applied.

4.3 Other applications

This database can benefit the study of the toxicity of nanomaterials exposure in various ways. For example, through searching the data stored in the database, researchers can find out what kinds of tests have been done. It is very useful, because not only can researchers acquire enough current available information, but they can also avoid duplicate studies. Moreover, the author information can be also utilized to boost the connection in this field. For instance, by matching the content of studies with their author information, researchers can easily find others working in a similar field. Furthermore, this database is also convenient for targeting useful literatures. Specifically, users can easily find out the studies and publications in which they are appeared. Compared with the conventional methods by using key words to search literatures, this method focusing on the studies themselves is more efficient. Based on the current structure of the database and amount of data stored inside, the main applications and benefits have been shown above. With the further development of database structure and storing of more data, an increasing number of applications will be developed.

5 Discussion

Building a database for nanomaterial exposure is an area not well addressed in the field of nanomaterial safety. The benefits of using this database can help to boost the development of this field. However, the database is currently only in its initial stage, and it needs to be further developed. The following discussion sections mainly focuses on several important parts influencing the performance of the database, and several key points and suggestions will be provided.

5.1 Database structure

The fundamental database structure has been already built, but it still needs to be optimized. Focus should be paid on three main factors that decide the database structure: tables, table contents, and the connections between tables.

Tables are the main content of the database, and they show important information of each study. In order to better manage tables, they are categorized into six sections, which include Material, Environmental System, Biological System, Functional Assay, Study_PI_Publiation and Study. Each section represents one aspect of exposure tests. On the other hand, these tables are not fixed, and more tables might be added into the database if necessary.

In addition to developing better tables to store data, table contents also need to be optimized. After data were curated for two types of nanomaterials (silver nanoparticles and CNTs), some fields in the table were found with nothing imported. For these redundant fields, it is necessary to carefully consider their importance and decide whether they should be removed from the table. As more types of data need to be imported, new table and table fields also need to be added. For example, for the material table, in addition to the normal parameters, other characters might be needed to describe new nanomaterials.

The table connection is the last part forming a database, and it is important to influence the efficiency of the data query process. For this part, efforts should be made to refine the connections and show the correct relation between every table. Typically, for databases with the same function, it is better for them to have fewer and clearer connections. For example, redundant table connections will cause errors in querying data and increase the difficulty of adding new tables or connections.

5.2 Data quality

In addition to the database structure, data quality is another important factor influencing the performance of the whole database. Data with good quality should be reliable and useful. Because the data usually come from published paper and directly from original principle investigators, the reliability of data is not hard to guarantee. However, the usability of the data is difficult to improve. In order to understand and solve this problem, it is necessary to deeply dig into it.

Normally, a small difference in doing the toxicological experiment will lead to huge difference in results. For example, just for CNTs themselves, factors like how they are

manufactured (including which catalysts were used, which manufacturing methods were applied, which precursors were chosen to produce CNTs, etc.); their size; and what kind of experimental preparation methods have been used will equip them with different characters. Moreover, exposure methods, for instance, whether the CNTs are exposed to organisms through water, air or direct injection, are also important to influence the toxicity of CNTs. In sum, nanomaterials from different sources should be regarded as different materials, even though they have the same name. The toxicological tests results for them should be also separately considered.

For this reason, some contradictory results have been published. For example, Wang et al. (2012) reported that MWCNTs exposure would not significantly increase the germination rate of wheat and are able to penetrate the root area cell membrane. However, contradictory results were published in Miralles et al., (2012), which showed not only that germination percentage of wheat significantly increased but also that there is no strong evidence showing that MWCNTs could penetrate into the cell membrane of wheat.

For better comparability of toxicological studies, test guidelines for the ecotoxicology and environmental fate of nanomaterials have been developed by OECD (2014). This guideline focuses on some important parts that might influence the toxicological test; however, it does not provide specific methods for analyzing the toxicity of nanomaterials (OECD, 2014). Therefore, this guideline is not so applicable and not widely used by researchers.

Developing a series of standardized test methods should be helpful not only for the comparison of different studies but also for the improvement of data usability for the database. Specifically, by applying this method, data will be more normative, and it is easier to find large amounts of data that can be integrated to do deeper analysis. In addition to standardizing the experimental methods, the manufacturing processes of nanomaterials should be also normalized. Each nanomaterial should be assigned a specific material name or number, which can benefit the data query process by effectively targeting specific nanomaterials.

On the other hand, because it is difficult to compare the toxicity of nanomaterials on different types of organisms (e.g. invertebrates, vertebrates, microorganisms, etc.), it is necessary to separately design standard experimental methods for each of them. For example, designing methods only for invertebrates, and making the toxicity of nanomaterials on invertebrates comparable. Furthermore, it might helpful to design a series of indices, which include results of some normal tests (e.g. biouptake, death rate) and other important biomarkers. Based on

analyzing these indices, a model can be developed to evaluate the toxicity of exposing a certain type of nanomaterial to an organism.

5.3 Data quantity

The amount of data imported into a database is another important factor when deciding whether it is a good database or not. Even with good data quality, a database is not useful without large amounts of data. Currently, a database builder personally imports all data into the database; however, this is not efficient. An more effective way is to build a platform, through which researchers can self-report the data into the database by some specific standards. This platform can help to save time for database builders. However, a good data censor mechanism should be built at the same time to avoid the importing of data with bad quality.

6 Conclusion

Nanomaterials have been proved to be very useful in various fields; however, the question of whether it is safe to use them is still under debate. The outcome of this project is to build a database for nanomaterials exposure, by which to help to answer the previous question in the following ways.

First of all, it can stimulate the wider spreading of the exposure data and create a more transparent research environment. A well-developed database can help users to swiftly query data that they need to do the research. Furthermore, based on data queried from various sources, further analysis can be conducted to explore the deeper mechanisms of nanomaterial toxicity and make synthetic conclusions. A database with a large amount of recently reported data can also help users to increase research efficiency and save limited resources by avoiding doing redundant studies.

Two types of nanomaterials exposure data have so far been imported to the database, and the database structure is designed to represent the studies of these two materials. Therefore, the structure needs to be further optimized not only to fit new nanomaterials but also to better realize the function of the whole database.

In addition to the structure, the data quality and quantity are not well developed to date, and they require more attention. The usability of data is an important factor influencing the data quality; however, usability is not optimal for the dataset already imported. In order to increase the data quality, a series of standards should be established. They might include conducting

standardized toxicological tests, manufacturing standardized nanomaterials, and importing normalized format of data. In addition to developing standardized methods, it might also helpful to design some indices, based on which to evaluate the impacts of nanomaterial exposure. For the increment of data quantity, a data-sharing platform needs to be built to encourage users to self-report data into the database. In this way, the data importing efficiency and accuracy can dramatically increase.

In sum, building a database for nanomaterial exposure is a new direction in the study of nanomaterial safety. Further development of this database promises to benefit research in the wider area of environmental pollutants exposure.

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Appendix

	Table Name			
	Materials	**Size**	**Surface Functionalization**	**Core**
Table Content	Matieral_id	Size_id	Surface_functionalization_id	Core_id
	Product_id	Measurement_type	Measurement_type	Measurement_type
	Core_id	Measurement_value	Measurement_value	Measurement_value
	Shell_id	Measurement_units	Measurement_units	Measurement_units
	SF_id	Uncertainty_value	Uncertainty_value	Uncertainty_value
	Dispersal_id	Uncertainty_units	Uncertainty_units	Uncertainty_units
	Surface_funct ion.._id	Distribution_type	Instrument_id	Instrument_id
	Size_id	Instrument_id	Detailed_method	Detailed_method
	Shape_id	Detailed_method	Reference	Reference
	Release_id	Reference	Examiner_id	Examiner_id
	…	Aspect_ratio	Composition	Composition

Table A. Content of three important tables in the Material section.

	Table Name			
	Environmental System	**Water**	**Air**	**Soil_Sediment**
Table Content	env_system_id	water_id	air_id	soil_sediment_id
	descriptor	descriptor	descriptor	descriptor
	water_id	dispersant_id	dispersant_id	dispersant_id
	soil_sediment_id			
	air_id			

Table B. Content of three second-order tables in the Environmental System section.

	Table Name			
	Biological System	**Invertebrate**	**Vertebrate**	**Plant**
Table Content	Invertebrate.id	Invertebrate.id	Veterbrate.id	Plant.id
	Veterbrate.id	Descriptor	Descriptor	Descriptor
	Plant.id			
	Invertebrate.id			
	…			

Table C. Content of four important tables in the section of Biological System.

	Table Name		
	Functional Assay	**Endpoint**	**Biouptake**
Table Content	Functional_assay_id	Endpoint_id	Biouptake_id
	Aggregation_id	Concentration_type	Rate
	Concentration_id	Concentration_value	Concentration
	Formation_id	Matrix	Detailed_method
	Dissolution_id	Organism	Reference
	Endpoint_id	Manufacturer	
	Attachment_id	Endpoint_type	
	Biouptake_id	Endpoint_value	
	Depuration_id	Endpoint_unit	
	Redox_id	Endpoint_uncertainty_value	
	Transformation_id	Endpoint_uncertainty_units	
		Hazard_level	

Table D. Content of the three example tables in the section of Functional Assay.

	Table Name			
	Study_PI_Publication	**PI**	**Publication**	**Institution**
Table Content	Study_pi_publication_id	Pi_id	Publication_id	Institution_id
	Study_id	Pi_first_name	Publication_title	Institution_name
	Pi_id	Pi_lase_name	Journal_name	Institution_dept
	Publication_id	Is_ceint	Publication_year	Insitution_city
			Author1_first_name	Institutio_state
			Author1_last_name	Institution_country
			Pulication_status	
			DOI_url	

Table E. Content of four important tables in the section of Study_PI_Publication

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